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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,695	02/04/2004	Paul D. Hanke	040049	4373

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EXAMINER

KIM, ALEXANDER D

ART UNIT	PAPER NUMBER
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1656

DATE MAILED: 11/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/771,695

Applicant(s)

HANKE ET AL.

Examiner

Alexander D. Kim

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 September 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-20 and 22-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19, 20, 22 and 24 is/are rejected.
- 7) ☒ Claim(s) 23 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 September 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-Final rejection (mailed on 06/02/2006), Applicants filed a response and amendment received on 09/05/2006. Said amendment cancelled Claims 1-18, 21, 25-32, amended Claims 19, 22 and 23. Thus, Claims 19-20 and 22-24 are pending in the instant Office action.

Examiner notes two typographical errors in the Applicants' instant arguments and remarks: (a) stating at page 7, top that Claim 24 is canceled (filed on 9/5/2006), however, the claim 24 is not cancelled in the amended claims, and is included in this office action; (b) "Support for the amendment to claim 20" (see Remarks on page 7 of 10, line 7) would appear to be ---Support for the amendment to claim 19--- because claim 19 has been amended, not claim 20.

Priority

2. As previously noted, the application claims the benefit of a divisional application of prior-filed U.S. applications 09/722,441 (filed on 11/28/2000), which claims benefit of provisional application 60/184,130 (filed on 02/22/2000) and 60/173,707 (filed on 12/30/1999) under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

Examiner suggests applicants update the status of priority application 09/722,441 which is now US patent 6,927,046.

Withdrawn-Objections to the Specification

3. Previous objection of the title is withdrawn by the virtue of Applicants' amendment.
4. Previous objection with the parenthesis "(I)" at the end of the protein sequence in Figure 24, which lacks description is withdrawn by the virtue of deleting the "(I)" in the Figure 24.
5. Previous objection in Figure 22 is withdrawn by the virtue of Applicants' amendment.

New-Objections to the Specification

6. The polypeptide of SEQ ID NO: 19 contains Ile122, which was deleted in Figure 24 by the amendment as described above. However, the Ile122 is still part of SEQ ID NO: 19 as shown in sequence listing. Also, the nucleic acid of SEQ ID NO: 18 has "AT" dinucleotide sequence at the end, which does not encode Ile122. The translation of AT into a Ile in the sequence listing and the description of replaced Figure 24 are unclear. Appropriate clarification is required.
7. The amendment filed on 09/05/2006 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added

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material which is not supported by the original disclosure is as follows: The amino acid sequence disclosed in Figure 24 without the C-terminal Ile do not have support in the original disclosure.

Applicant is required to cancel the new matter in the reply to this Office Action.

New-Objections to the Claims

8. Claim 19 should have status of ---Currently Amended--- instead of "(Previously Presented)". Applicant is reminded of the amendment practice according to MPEP 714 and 37 CFR 1.121.

9. Claim 23 is objected to because of the following informalities: The use of "The host cell" should be changed to ---A host cell--- to improve format of Claim 23.

Maintained-Objections to the Specification

10. Previous objection of the Abstract is maintained because it continues to disclose no information regarding to the encoded protein (hypothetical protein) by the gene ORF2. Appropriate correction is required.

Withdrawn-Claim Rejections - 35 USC § 112

11. Previous rejection of Claims 19-22 and 24 under 35 U.S.C. § 112, first paragraph, written description, is withdrawn by the virtue of applicants' amendment.

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12. Previous rejection of Claims 19-22 and 24 under 35 U.S.C. 112, first paragraph, scope of enablement is withdrawn by the virtue of applicants' amendment.

13. Previous rejection of Claim 23 under 35 U.S.C. 112, first paragraph, enabling deposit, is withdrawn by the virtue of applicants' statement, page 8, lines 6-11.

New Matter

14. Claims 19-20, 22, and 24 are rejected under 35 U.S.C. 112, first paragraph, new matter, as failing to comply with the written description requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection and is necessitated by amendment.

Claim 19 (claims 20, 22 and 24 depend therefrom) is amended by adding the limitation "wherein said polynucleotide molecule is integrated into the chromosome of a cell of the genus *Corynebacterium*" as shown in the amended claims (filed on 09/05/2006). Applicants disclose "Support for the amendment to claim 20 is found at least on page 4, line 21". This statement appears to have been intended as showing support for claim 19, not claim 20. Thus, said support has been treated as support for claim 19 in this office action. The instant specification on page 4, line 21 states "SEQ ID NO: 2, wherein said isolated polynucleotide molecule is integrated into said host cell's chromosome" (see page 4, lines 22-23). This disclosure fails to support the nucleic acid

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isolated polynucleotide of Claim 19. Applicant is invited to show support for Claim 19 in the application as filed.

15. Claim 24 is rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for transforming a *Corynebacterium* species host cell with a vector comprising a polynucleotide encoding SEQ ID NO: 19, however, does not reasonably provide enablement for a method of transforming a *Corynebacterium* species host cell with a chromosome of a *Corynebacterium* with a nucleic acid encoding SEQ ID NO: 19 integrated therein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The Court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of

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experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The nature of invention is drawn to a method of transforming a *Corynebacterium* species host cell with a vector comprising a transposon and a polynucleotide molecule encoding SEQ ID NO: 19, which incorporates the gene into a chromosome of the host cell after transformation with said vector. The breadth of Claim 24 is so broad as to encompass a method of transforming a host cell with a whole chromosome having a nucleic acid encoding SEQ ID NO: 19 integrated therein. However, the specification and prior art do not teach a method of transforming the whole chromosome into a host species. The specification provides no working example of transforming a host using a whole chromosome. Because there is no direction or guidance regarding transforming a *Corynebacterium* species with a whole chromosome, it is highly unpredictable as to whether a skilled artisan could achieve such transformation. For at least the reasons set \ undue experimentation would be required for a skilled artisan to make and use the entire scope of the claimed invention.

Withdrawn-Claim Rejections - 35 USC § 102

16. Previous rejection of Claims 19-20 and 22 under 35 U.S.C. 102(b) as being anticipated by Pisabarro et al. is withdrawn by the virtue of Applicants' amendment.

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Said amendment added a limitation of the polynucleotide integrated into the chromosome of a *Corynebacterium*. The Pisabarro et al. reference does not teach said added limitation.

Withdrawn-Claim Rejections - 35 USC § 103

17. Previous rejection of Claim 24 under 35 U.S.C. 103(a) as being unpatentable over Pisabarro et al. in view of Serworld-David et al. is withdrawn by the virtue of Applicants' amendment. Said amendment added a limitation of the polynucleotide integrated into the chromosome of a *Corynebacterium*. Pisabarro et al. and Serworld-David et al. do not teach or suggest said added limitation.

New-Claim Rejections - 35 USC § 103

18. Claims 19-20, 22, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pisabarro et al. (1993 May, Journal of Bacteriology, Vol. 175, pp. 2743-2749 as cited in IDS) in view of Labarre et al (1993, Journal of Bacteriology, Vol. 175, p. 1001-1007) and Hirano et al. (US Pat. 6,090,597, Jul 18, 2000). This rejection is necessitated by amendment.

Pisabarro et al. disclose the teaching as described in the previous office action. See pages 9-10. Pisabarro et al. suggest that "it is likely that ORF2 is also translated in *corynebacteria*" in lysine biosynthesis (see bottom left column, last paragraph on pp. 2748).

Pisabarro et al. do not teach integrating said polynucleotide into the chromosome of a *Corynebacterium*.

Hirano et al. teach successful results to improve "L-lysine productivity" can be "obtained by the means of amplification of genes for the L-lysine biosynthesis" in a *Corynebacterium* host cell (see column 1, lines 42-44).

Labarre et al. teach a "reliable and general method" (see Material and Methods" on page 1001-1002 and page 1006, left column bottom) for inserting genes into the chromosome of *C. glutamicum*. According to Labarre et al., chromosomal integration enhances expression of encoded protein (Table 3) and suggest the technique can be used "in studying and eventually modifying complex host functions such as high-level amino acid production" (see p. 1007, left column, top).

Therefore, It would have been obvious to one of ordinary skill in the art at the time the invention was made to integrate the orf2 gene, as taught by Pisabarro et al. One would have been motivated to integrate the Orf2 nucleic acid of Pissabarro et al. into the chromosome of a *Corynebacterium* in order to determine if increased expression of Orf2 resulted in increased L-lysine production because of the teachings of Pissabarro et al. and Hirano et al. and would have used the method of Labarre et al. because the method is reliable, enhances protein expression and can be used for studying amino acid production as taught by Labarre et al. into the chromosome of *C. glutamicum* by the method of Labarre et al. One would have had a reasonable expectation of success for the insertion of the orf2 gene of Pissabarro et al. into the chromosome of a *Corynebacterium* host cell because of the teachings of Pissabarro et

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al. and Labare et al. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Withdrawn-Double Patenting

19. Previous rejection of Claims 19-22 and 24 on the ground of nonstatutory double patenting over claims 11-13 and 48 of U. S. Patent No. 6,927,046, is withdrawn by the applicants' response stating that the instant claims were restricted in the parent application.

Summary of Pending Issues

20. The following is a summary of the issues pending in the instant application:

- a. The specification is objected because of the nucleic acid of SEQ ID NO: 18 have "AT" dinucleotide sequence at the end, which does not encode Ile122. The translation of AT into a Ile in the sequence listing and the description of replaced Figure 24 are unclear.
- b. The specification is objected because of the new matter is introduced in the amino acid sequence in Figure 24.
- c. Claim 19 is objected because of wrong status in amended claims.
- d. Claim 23 is objected for informality.
- e. The objection of the Abstract is maintained.
- f. Claims 19-20, 22, 24 are newly rejected under 35 U.S.C. 112, first paragraph, new matter, as failing to comply with the written description requirement.
- g. Claim 24 is newly rejected under 35 U.S.C. 112, first paragraph, scope of enablement.
- h. Claims 19-20, 22, 24 is newly rejected under 35 U.S.C. 103(a) as being unpatentable over Pisabarro et al. in view of Labarre et al.

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Conclusion

21. Claims 19-20, 22, and 24 are not allowed for the reasons identified in the numbered sections of this Office action. Claim 23 is objected. Applicants must respond to the objections/rejections in each of the numbered section in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander D. Kim whose telephone number is (571) 272-5266. The examiner can normally be reached on 8AM-5PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alexander Kim
November 13, 2006


DAVID J. STEADMAN, PH.D.
PRIMARY EXAMINER